

## REMARKS

### I. Amendments

Claim 24 has been amended as follows:

- a) The limitation of claim 25 relating to the treatment of a cartilage or osteochondral defect has been introduced;
- b) The reference to the acronym CXCL6 has been replaced with a reference to the full name “Chemokine , CXC motif, Ligand 6” and reference to the acronym is placed between parenthesis;
- c) The article “an” has been added between “to” and “individual;” and
- d) The phrase “administering an effective amount of Chemokine, CXC Motif, Ligand 6 (CXCL6) to an individual in need thereof, so as to obtain promotion of hyaline cartilage in said cartilage defects and optionally subchondral bone formation in said osteochondral defects” has been added.

This latter amendment is based, for example, on the specification at page 5, lines 18-24:

*A further finding of the present invention is that CXCL6 is involved in the restoration of osteochondral defects. Thus, contrary to the involvement of chemokines in cartilage degradation as described in the prior art, the present invention relates to the use of CXCL6 and CXCL6 expressing cells in the formation of cartilage or bone in vitro or in vivo and in the repair of cartilage or osteochondral defects. (emphasis added).*

And on page 13, lines 8 to 10 of the specification, which states:

*A cartilage defect is referred to as an osteochondral defect when there is damage to articular cartilage and underlying (subchondral) bone.*

This passage supports the fact that, where the cartilage defect is an osteochondral defect, subchondral bone formation is also affected.

Claim 25 has been cancelled.

In claim 26, the reference to "prevention" has been deleted.

Claim 26 has been amended to refer to recombinant CXCL6 rather than specifying that the source of CXCL6 is CXCL6-expressing cells. Support for this amendment is found in the specification which states, on page 6, lines 2-4:

*The source of CXCL6 according to this aspect of the invention can be either natural, recombinant or synthetic.*

Claim 28 is amended by replacing the wording "*in a gradient*" with "*in a concentration gradient*" and amending the order of the words to improve the clarity of the claims.

Support for this amendment is found in the specification, for example, in the passage spanning from page 19, line 28, to page 20, line 3:

*According to a particular embodiment of the present invention the matrix allows administration of CXCL6 "**in a gradient to the osteochondral defect**", The gradient can correspond to the variable degree of repair needed in the defect and/or to the transition of cartilage (low concentration) to bone (high concentration). Gradients of CXCL6 can be applied for example by using matrices with a gradient in pore size. Filling such a matrix with a polymerisable solution with CXCL6 will result in a "**concentration gradient**" of CXCL6. (emphasis added.)*

New claim 39 has been added. Support for this claim is found throughout the specification, more particularly in the section spanning page 12, line 30 to page 13, line 1:

*A '**cartilage defect**' as used herein relates to a defect which involves the destruction of cartilage (also referred to as a cartilage defect). Particular cartilage defects*

*envisaged in the context of the present invention are joint surface defects.*

## II. Claim objections

The Examiner has objected to claims 24, 27, and 28 for use of the acronym “CXCL6” without first defining what it represents in the independent claims. It is submitted that the present amendment to the claims renders this objection moot.

The Examiner has objected to claim 24, in view of the wording used. Applicants have amended claim 24, as suggested by the Examiner, by introducing the term “an” prior to “individual”. This objection should therefore be withdrawn

## III. Claim rejections

### **A. Rejections under 35 USC §112, second paragraph**

The Examiner has rejected, in item 5 of the Action, claims 24-29 under 35 USC §112, second paragraph, as being indefinite for reciting elements as improper Markush groups. Without acquiescence to this rejection, Applicants have amended claim 24 and this rejection should therefore be withdrawn.

The Examiner has rejected, in item 6 of the Action, claims 24-29 under 35 USC §112, second paragraph, as being indefinite for failing to provide a step which clearly relates back to the preamble. Without acquiescence to this rejection, Applicants have amended claim 24 to include in the administration step, a reference to the preamble. Indeed, claim 24 now states:

24. A method for treatment of a cartilage or osteochondral defect comprising the step of administering an effective amount of Chemokine, CXC Motif, Ligand 6 (CXCL6) to an individual in need thereof, so as to obtain promotion of hyaline cartilage in said cartilage defects and optionally subchondral bone formation in said osteochondral defects. (emphasis added)

It is submitted this rejection should be rendered moot by the present amendment to the claims.

The Examiner has rejected, in item 7 of the Action, claim 27 under 35 USC §112, second paragraph, as being indefinite for referring to the “source of CXCL6” without appropriate antecedent basis for this terminology in claim 24. Without acquiescence to this rejection, Applicants have amended claim 27 to no longer refer to the source of CXCL6 but to refer to “recombinant CXCL6”. This rejection should therefore be withdrawn.

The Examiner has rejected, in item 8 of the Action, claims 24, 27-29 under 35 USC §112, second paragraph, as being indefinite for referring to both a method of treatment and a method for the promotion of cartilage and/or bone formation. Without acquiescence to this rejection, Applicants have amended claim 24 to refer to “a method for the treatment of a cartilage or osteochondral defect,” while specifying that this is achieved through the promotion of cartilage and optionally bone formation, in the characterizing portion of the claim. This rejection should therefore also be withdrawn.

The Examiner has rejected, in item 9 of the Action, claims 25 and 26 under 35 USC §112, second paragraph, as being indefinite for referring to prevention in the absence of an antecedent basis for this term in independent claim 24. Claim 25 has been cancelled.

Without acquiescence to this rejection, Applicants have removed the reference to “prevention” in claim 26 and this basis of the rejection should therefore be withdrawn.

The Examiner has rejected, in item 10 of the Action, claim 28 under 35 USC §112, second paragraph, as being indefinite for referring to the term “a gradient,” which is considered a relative term. Without acquiescence to this rejection, Applicants have amended claim 28 to refer to “a concentration gradient”. As indicated by the Examiner, the specification provides in the section on page 20, methods by which such a concentration gradient of CXCL6 are obtained.

**B. Rejections under 35 USC §112, first paragraph**

The Examiner has rejected, in item 11 of the Action, claims 24-29 under 35 USC §112, first paragraph. The Examiner states: “*Claims 24-29 are rejected under 35 USC 112, first paragraph, because the specification, while being enabling for a method for the production of **hyaline** cartilage and **subchondral** bone formation comprising administering an effective amount of CXCL6 to promote hyaline cartilage and subchondral bone formation, does not reasonably provide enablement for a method of treatment for the promotion of cartilage and/or bone formation comprising the step of administering an effective amount of CXCL6 to an individual in need thereof.* (emphasis added)

Without acquiescence to this rejection, Applicants have amended claim 24 to refer to methods which result in the formation of “hyaline cartilage” and to “subchondral bone”.

Accordingly, it is submitted that the present amendment to the claims renders this rejection moot.

The Examiner has further rejected the claims for referring to the prevention of a cartilage or osteochondral defect. This aspect of the rejection under 35 USC §112, first paragraph should be rendered moot by the present amendments to the claims, by which reference to the term “prevention” has been removed.

The Examiner has rejected, in item 12 of the Action, claim 29 under 35 USC §112, first paragraph as failing to comply with the written description requirement. The Examiner alleges that the specification fails to provide any distinguishing identifying characteristics of the genus of “chondrogenic cells.”

Applicants respectfully disagree. As indicated by the Examiner, the term “chondrogenic” implies and is defined in the specification (on page 10 line 31 to page 12 line 1) “*cells capable of producing stable hyaline cartilage.*” It is submitted that the ability of the cell to produce stable hyaline cartilage corresponds to the “particular function” which is to be conserved as required by the Examiner (page 9, lines 18-19 of the Action).

### **C. Rejections under 35 USC §102**

The Examiner has rejected, in item 13 of the Action, claim 24 under 35 USC §102 as being anticipated by Van Damme et al. (US 5,840,524). The Examiner has specified that the recitation “for promotion of cartilage and/or bone defects” has not been given patentable

weight because the recitation occurs in the preamble.

The claims, as presently amended, now refer to a method *“comprising the step of administering an effective amount of "Chemokine, CXC Motif, Ligand 6" (CXCL6) to an individual in need thereof, so as to obtain promotion of hyaline cartilage in said cartilage defect and optionally subchondral bone formation in said osteochondral defects”*.

Van Damme et al. does not describe the administration of CXCL6 so as to obtain promotion of hyaline cartilage and optionally subchondral bone formation in cartilage and osteochondral defects. Accordingly, it is submitted that the present amendment renders the Examiner’s rejection moot.

The Examiner further refers to prior art made of record and not considered pertinent to the Applicant’s disclosure. It is submitted that each of these references equally refer to the use of CXCL6 as expressed by chondrogenic cells. None of the cited references discloses the administration of CXCL6 so as to obtain promotion of hyaline cartilage and optionally subchondral bone formation in cartilage or osteochondral defects. Accordingly, it is submitted that the disclosure of these references is not relevant to the claims as presently amended.

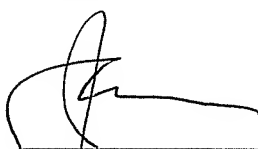
CONCLUSION

Applicants submit that the claims are in condition for allowance, and such action is respectfully requested.

If there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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